AMENDMENT

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (currently amended) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region a direct agonist of ~~an ATP-sensitive~~ a calcium-activated potassium channel, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and administering to the subject, simultaneously or substantially simultaneously with the direct agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claim 2. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke or ischemia.

Claim 3. (previously presented) The method of Claim 1, wherein the abnormal brain region is a region of tumor tissue.

Claims 4-11 (cancelled)

Claim 12. (previously presented) The method of Claim 1, wherein the mammal is a human.

Claim 13. (previously presented) The method of Claim 1, wherein the medicant is a therapeutic cytotoxic agent or anticancer chemotherapeutic agent.

Claims 14-17 (cancelled)

Claim 18. (previously presented) The method of Claim 1, wherein the direct agonist is administered by intravenous or intra-arterial infusion or injection.

Claim 19. (previously presented) The method of Claim 1, wherein the direct agonist is administered by intracarotid infusion or injection.

Claim 20. (previously presented) The method of Claim 1, wherein the direct agonist is administered to the mammalian subject by an intravenous infusion.

Claim 21. (previously presented) The method of Claim 1, wherein the direct agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

Claim 22. (previously presented) The method of Claim 21, wherein the direct agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

Claim 23. (previously presented) The method of Claim 1, wherein the direct agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100$\mu g\ kg^{-1}\ min^{-1}$ for up to about 30 minutes.

Claim 24. (previously presented) The method of Claim 23, wherein the direct agonist is administered to the mammalian subject in a bolus injection.

Claims 25-47 (cancelled)

Claim 48. (currently amended) A method of delivering a medicant to a malignant tumor in a mammalian subject, comprising: administering to a mammalian subject having a malignant

tumor a direct agonist of ~~an ATP-sensitive~~ a calcium-activated potassium channel, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the malignant tumor; and administering to the subject, simultaneously or substantially simultaneously with the direct agonist the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

Claims 49-56 (cancelled)

Claim 57. (original) The method of Claim 48, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodetermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma or carcinoma.

Claim 58. (original) The method of Claim 48, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

Claim 59. (currently amended) The method of Claim 48, wherein said mammal is a human.

Claim 60. (previously presented) The method of Claim 48, wherein the medicant is a therapeutic cytotoxic agent or anticancer chemotherapeutic agent.

Claims 61-64 (cancelled)

Claim 65. (previously presented) The method of Claim 48, wherein the direct agonist is administered by intravenous or intra-arterial infusion or injection.

Claim 66. (previously presented) The method of Claim 48, wherein the direct agonist is administered by intracarotid infusion or injection.

Claim 67. (previously presented) The method of Claim 48, wherein the direct agonist is administered to the mammalian subject intravenous infusion.

Claim 68. (previously presented) The method of Claim 48, wherein the direct agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

Claim 69. (currently amended) The method of Claim ~~68~~ 48, wherein the direct agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

Claim 70. (currently amended) The method of Claim ~~68~~ 48, wherein the direct agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100μg kg^{-1} min^{-1} for up to about 30 minutes.

Claim 71. (previously presented) The method of Claim 70, wherein the direct agonist is administered by bolus injection.

Claims 72-134 (cancelled)

Claim 135. (currently amended) A pharmaceutical composition comprising a combination of a direct agonist of ~~an ATP-sensitive~~ a calcium-activated potassium channel, formulated in a pharmaceutically acceptable solution together with a medicant selected from the group consisting of therapeutic cytotoxic agents or anticancer chemotherapeutic agents for delivery by intravascular infusion or injection into a mammal.

Claim 136. (currently amended) The pharmaceutical composition of Claim 135, wherein the direct agonist ~~of an ATP-sensitive potassium channel~~ is present in an amount of about 0.075 to 1500 micrograms-per kilogram body.

Claim 137. (previously presented) The pharmaceutical composition of Claim 135, wherein the direct agonist is present in an amount of about 0.075 to 150 micrograms per kilogram body mass.

Claims 138-150 (cancelled)

Claim 151. (original) The pharmaceutical composition of Claim 135, further comprising a buffer solution pharmaceutically acceptable for intravascular infusion into an animal.

Claim 152. (original) The pharmaceutical composition of Claim 151, wherein the buffer solution is phosphate buffered saline.

Claim 153. (currently amended) A kit for enhancing the delivery of a medicant to an abnormal brain region and/or to a malignant tumor, comprising: a direct agonist of ~~an ATP-sensitive~~ a calcium-activated potassium channel; and instructions for using the direct agonist for enhancing the delivery of a medicant to an abnormal brain region or to a malignant tumor.

Claims 154-194 (cancelled)

Claim 195. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by stroke.

Claim 196. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by ischemia.

Claim 197. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury or trauma.

Claim 198. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by infection.

Claim 199. (original) The method of Claim 1, wherein the abnormal brain region is a region of benign tumor tissue.

Claim 200. (original) The method of Claim 1, wherein the abnormal brain region is a region of malignant tumor tissue.

Claim 201. (original) The method of Claim 1, wherein the abnormal brain region includes a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

Claim 202. (original) The method of Claim 1, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

Claim 203. (original) The method of Claim 1, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

Claim 204. (original) The method of Claim 1, wherein the medicant is a protein.

Claim 205. (original) The method of Claim 1, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

Claim 206. (original) The method of Claim 1, wherein the medicant is a cytokine, cytokine antagonist, or cytokine agonist.

Claim 207. (original) The method of Claim 1, wherein the medicant is an interferon.

Claim 208. (original) The method of Claim 1, wherein the medicant is an interleukin.

Claim 209. (original) The method of Claim 208, wherein the interleukin is interleukin 2.

Claim 210. (currently amended) The method of Claim 1, wherein the medicant is a transforming growth factor.

Claim 211. (original) The method of Claim 210, wherein the transforming growth factor is transforming growth factor-β

Claim 212. (original) The method of Claim 1, wherein the medicant is tumor necrosis factor-α.

Claim 213. (original) The method of Claim 1, wherein the medicant is an antimicrobial agent or an antibiotic.

Claim 214. (original) The method of Claim 1, wherein the medicant is an immunotoxin or immunosuppressant

Claim 215. (original) The method of Claim 1, wherein the medicant is a boron compound.

Claim 216. (original) The method of Claim 1, wherein the medicant is an ischemia-protective agent.

Claim 217. (currently amended) The method of Claim ~~X~~ 216, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

Claim 218. (original) The method of Claim 1, wherein the medicant is an adrenergic agent.

Claim 219. (original) The method of Claim 1, wherein the medicant is an anticonvulsant.

Claim 220. (original) The method of Claim 1, wherein the medicant is an anti-trauma agent.

Claim 221. (original) The method of Claim 1, wherein the medicant is cisplatin or carboplatin.

Claim 222. (original) The method of Claim 1, wherein the medicant is methotrexate.

Claim 223. (original) The method of Claim 1, wherein the medicant is 5-flourouracil.

Claim 224. (original) The method of Claim 1, where the medicant is amphotericin.

Claim 225. (original) The method of Claim 1, wherein the medicant is daunorubicin.

Claim 226. (original) The method of Claim 1, wherein the medicant is doxorubicin.

Claim 227. (original) The method of Claim 1, wherein the medicant is vincristine.

Claim 228. (original) The method of Claim 1, wherein the medicant is vinblastine.

Claim 229. (original) The method of Claim 1, wherein the medicant is busulfan.

Claim 230. (original) The method of Claim 1, wherein the medicant is chlorambucil.

Claim 231. (original) The method of Claim 1, wherein the medicant is cyclophosphamide.

Claim 232. (original) The method of Claim 1, wherein the medicant is melphalan.

Claim 233. (original) The method of Claim 1, wherein the medicant is ethyl ethanesulfonic acid.

Claim 234. (currently amended) The method of Claim 1, wherein the medicant is a diagnostic agent.

Claims 235-239 (cancelled)

Claim 240. (original) The method of Claim 48, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

Claim 241. (original) The method of any Claim 48, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

Claim 242. (original) The method of Claim 48, wherein the medicant is a protein.

Claim 243. (original) The method of Claim 48, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

Claim 244. (original) The method of Claim 48, wherein the medicant is a cytokine, cytokine antagonist, or cytokine agonist.

Claim 245. (original) The method of Claim 48, wherein the medicant is an interferon.

Claim 246. (original) The method of Claim 48, wherein the medicant is an interleukin.

Claim 247. (original) The method of Claim 247, wherein the interleukin is interleukin 2.

Claim 248. (currently amended) The method of Claim 48, wherein the medicant is a transforming growth factor.

Claim 249. (original) The method of Claim 248, wherein the transforming growth factor is transforming growth factor-β.

Claim 250. (original) The method of Claim 48, wherein the medicant is tumor necrosis factor-α.

Claim 251. (original) The method of Claim 48, wherein the medicant is an antimicrobial agent or an antibiotic.

Claim 252. (original) The method of Claim 48, wherein the medicant is an immunotoxin or immunosuppressant.

Claim 253. (original) The method of Claim 48, wherein the medicant is a boron compound.

Claim 254. (original) The method of Claim 48, wherein the medicant is an ischemia-protective agent.

Claim 255. (currently amended) The method of Claim ~~255~~ 254, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

Claim 256. (original) The method of Claim 48, wherein the medicant is an adrenergic agent.

Claim 257. (original) The method of Claim 48, wherein the medicant is an anticonvulsant.

Claim 258. (original) The method of Claim 48, wherein the medicant is an anti-trauma agent.

Claim 259. (original) The method of Claim 48, wherein the medicant is cisplatin or carboplatin.

Claim 260. (original) The method of Claim 48, wherein the medicant is methotrexate.

Claim 261. (currently amended) The method of Claim 48, wherein the medicant is 5-flouroouracil.

Claim 262. (original) The method of Claim 48, where the medicant is amphotericin.

Claim 263. (original) The method of Claim 48, wherein the medicant is daunorubicin.

Claim 264. (original) The method of Claim 48, wherein the medicant is doxorubicin.

Claim 265. (original) The method of Claim 48, wherein the medicant is vincristine.

Claim 266. (original) The method of Claim 48, wherein the medicant is vinblastine.

Claim 267. (original) The method of Claim 48, wherein the medicant is busulfan.

Claim 268. (original) The method of Claim 48, wherein the medicant is chlorambucil.

Claim 269. (original) The method of Claim 48, wherein the medicant is cyclophosphamide.

Claim 270. (original) The method of Claim 48, wherein the medicant is melphalan.

Claim 271. (original) The method of Claim 48, wherein the medicant is ethyl ethanesulfonic

Claim 272. (original) The method of Claim 48, wherein the medicant is a diagnostic agent.

Claim 273-277 (cancelled)

Claim 278. (original) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is cisplatin or carboplatin.

Claim 279. (original) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is methotrexate.

Claim 280. (currently amended) The pharmaceutical composition of Claim 135, wherein the therapeutic catatonic agent is 5-fluoroureacil.

Claim 281. (original) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is amphotericin.

Claim 282. (original) The pharmaceutical composition of Claim 135, wherein the anticancer chemotherapeutic agent is daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

Claim 283. (currently amended) A pharmaceutical composition comprising a combination of a direct agonist of ~~an ATP-sensitive~~ a calcium-activated potassium channel formulated together in a pharmaceutically acceptable solution together with a ~~drug~~ medicant for delivery by intravascular infusion or injection, wherein the ~~drug~~ medicant is an antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anticonvulsant, anti-trauma agent or diagnostic agent.

Claim 284. (currently amended) A pharmaceutical composition comprising a combination of a direct agonist of ~~an ATP-sensitive~~ calcium-activated potassium channel formulated together in a pharmaceutically acceptable solution together with a ~~drug~~ medicant for delivery by intravascular infusion or injection, wherein the ~~drug~~ medicant is a naked DNA expression vector, protein, oligonucleotide or nucleotide analog.

Claims 285-286 (cancelled)

Claim 287. (new) The method of Claim 1, wherein the direct agonist is NS1619.

Claim 288. (new) The method of Claim 1, wherein the direct agonist is EBIO.

Claim 289. (new) The method of Claim 1, wherein the medicant is a DNA expression vector.

Claim 290. (new) The method of Claim 1, wherein the medicant is a viral vector.

Claim 291. (new) The method of Claim 290, wherein the viral vector is a therapeutic adenoviral vector or herpes simplex viral vector.

Claim 292. (new) The method of Claim 1, wherein the medicant is an oligonucleotide or nucleotide analog.

Claim 293. (new) The method of Claim 48, wherein the direct agonist is NS1619.

Claim 294. (new) The method of Claim 48, wherein the direct agonist is EBIO.

Claim 295. (new) The method of Claim 48, wherein the medicant is a DNA expression vector.

Claim 296. (new) The method of Claim 48, wherein the medicant is a viral vector.

Claim 297. (new) The method of Claim 48, wherein the viral vector is a therapeutic adenoviral vector or herpes simplex viral vector.

Claim 298. (new) The method of Claim 48, wherein the medicant is an oligonucleotide or nucleotide analog.

Claim 299. (new) The pharmaceutical composition of Claim 135, wherein the direct agonist is NS1619.

Claim 300. (new) The pharmaceutical composition of Claim 135, wherein the direct agonist is EBIO.

Claim 301. (new) The kit of Claim 153, wherein the direct agonist is NS1619.

Claim 302. (new) The kit of Claim 153, wherein the direct agonist is EBIO.

Claim 303. (new) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering YC-1 to a mammalian subject having an abnormal brain region, under conditions and in an amount sufficient, to increase the permeability

to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and administering to the subject, simultaneously or substantially simultaneously with YC-1 the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to the normal brain region.

Claim 304 (new) The method of Claim 303, wherein YC-1 is administered by intravenous, intra-arterial, or intracarotid infusion or injection.

Claim 305. (new) The method of Claim 303, wherein the mammal is a human.

Claim 306. (new) The method of Claim 303, wherein the abnormal brain region is a region a tissue physiologically affected by stroke or ischemia.

Claim 307. (new) The method of Claim 303, wherein the abnormal brain region is a region of tumor tissue.

Claim 308. (new) The method of Claim 303, wherein the abnormal brain region is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

Claim 309. (new) The method of Claim 303, wherein the medicant is a therapeutic cytotoxic agent or an anticancer chemotherapeutic agent.

Claim 309. (new) The method of Claim 309, wherein the therapeutic cytotoxic agent is cisplatin, carboplatin, methotrexate, 5-fluorouracil, amphotericin.

Claim 310. (new) The method of Claim 309, wherein the anticancer chemotherapeutic agent is daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

Claim 311. (new) The method of Claim 303, wherein the medicant is a antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anticonvulsant, anti-trauma agent or diagnostic agent.

Claim 312. (new) The method of Claim 303, wherein the medicant is a DNA expression vector, viral vector, protein, oligonucleotide or nucleotide analog.

Claim 313. (new) The method of Claim 303, wherein the medicant is a diagnostic agent.

Claim 314. (new) A pharmaceutical composition comprising a combination of YC-1, formulated in a pharmaceutically acceptable solution together with a therapeutic cytotoxic agent or anticancer chemotherapeutic agent for delivery by intravascular infusion or injection into a mammal.

Claim 315. (new) The pharmaceutical composition of Claim 314, wherein YC-1 is present in an amount of about 0.075 to 1500 micrograms per kilogram body mass.

Claim 316. (new) The pharmaceutical composition of Claim 314, wherein the therapeutic cytotoxic agent is cisplatin, carboplatin, methotrexate, 5-fluorouracil, or amphotericin.

Claim 317. (new) The pharmaceutical composition of Claim 314, wherein the anticancer chemotherapeutic agent is daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

Claim 318. (new) The pharmaceutical composition of Claim 314, further comprising a buffer solution pharmaceutically acceptable for intravascular infusion into a mammal.

Claim 319. (new) A pharmaceutical composition comprising YC-1 formulated together in a pharmaceutically acceptable solution together with a medicant for delivery by intravascular infusion or injection, wherein the medicant is an antimicrobial agent, antibiotic, interferon,